

# Etoposide phosphate

**Brand Name:** Etopophos (phosphate salt), Toposar, VePesid



## Drug Description

Etoposide is a semisynthetic podophyllotoxin-derived antineoplastic agent. [1]

## HIV/AIDS-Related Uses

Etoposide is currently being investigated to determine its safety and efficacy in treating AIDS-related non-Hodgkin lymphoma.[2] [3] [4] [5] Etoposide is also used to treat AIDS-related Kaposi's sarcoma.[6]

## Non-HIV/AIDS-Related Uses

Etoposide is indicated in combination with other antineoplastics for first-line treatment of testicular tumors. Etoposide is also indicated in combination with other agents for first-line treatment of small-cell lung carcinoma.[7]

## Pharmacology

The mechanism of action of etoposide is not fully understood; however, its cytotoxic effects appear to be produced by inhibiting DNA or altering DNA synthesis. Etoposide also appears to be cell-cycle dependent and cell-cycle specific, inducing G2-phase arrest and preferentially killing cells in the G2 and S phases. Although in vitro cytotoxicity of etoposide phosphate is significantly less than that produced by etoposide, once the salt form is dephosphorylated in vivo, its mechanism of action is equivalent to that of the base form.[8]

Etoposide is variously absorbed following oral administration, depending on dosage formulation. The absolute bioavailability of etoposide in liquid-filled soft gelatin capsules averages 50%, with a range of 25% to 75%. With this formulation, peak plasma concentrations (C<sub>max</sub>) of etoposide are achieved within 1 to 1.5 hours. C<sub>max</sub> and area under the plasma concentration-time curve (AUC) for this formulation vary but are consistently within the same range as those following an IV dose half as large. Following oral administration of 160 or 200 mg/m<sup>2</sup> soft gelatin capsules, peak plasma etoposide concentrations of 9 mcg/ml and 9.6 mcg/ml, respectively, were attained.[9]

Following IV administration of etoposide phosphate, the drug is rapidly absorbed and completely converted to etoposide in plasma. Clinical studies directly comparing the pharmacokinetic parameters of etoposide and etoposide phosphate showed no statistically significant difference in the etoposide plasma C<sub>max</sub> or AUC of the two formulations.[10]

As with oral formulations, absorption of IV etoposide varies markedly among patients. Over a dose range of 100 to 600 mg/m<sup>2</sup>, plasma C<sub>max</sub> and AUC increase linearly with dose. In adults with normal renal and hepatic function, an 80 mg/m<sup>2</sup> IV dose given over 1 hour averaged an etoposide plasma C<sub>max</sub> of 14.9 mcg/ml. Following 500 mg/hour IV infusions of 400, 500, or 600 mg/m<sup>2</sup>, etoposide plasma peak concentrations of 26 to 53, 27 to 73, and 42 to 114 mcg/ml, respectively, were attained. With continuous IV infusion of 100 mg/m<sup>2</sup> daily for 72 hours, plasma drug concentrations of 2 to 5 mcg/ml were reached 2 to 3 hours after the start of infusion and were maintained until the end of infusion. In children aged 3 months to 16 years with normal renal and hepatic function, IV infusions of 200 to 250 mg/m<sup>2</sup> given over 0.5 to 2.25 hours resulted in peak serum etoposide concentrations ranging from 17 to 88 mcg/ml.[11]

Following IV administration, etoposide undergoes rapid distribution. Apparent steady-state volume averages 20% to 28% of body weight or 7 to 17 L/m<sup>2</sup> in adults and 5 to 10 L/m<sup>2</sup> in children. IV etoposide is distributed minimally into pleural fluid and has been detected in saliva, liver, spleen, kidney, myometrium, healthy brain tissue, and brain tumor tissue. Etoposide and its metabolites do not readily penetrate the central nervous system. Concentrations of etoposide in cerebrospinal fluid range from undetectable to less than 5% of concurrent plasma concentrations during the initial 24 hours after IV administration, even with high doses. In vitro, etoposide is approximately 94% bound to serum proteins at a concentration of 10 mcg/ml.[12]

Etoposide is in FDA Pregnancy Category D; it can cause fetal harm when administered to a pregnant

# Etoposide phosphate

## Pharmacology (cont.)

---

woman. The drug has been shown to have severe teratogenic effects in laboratory animals and is therefore likely to be teratogenic in humans. If etoposide is used during pregnancy, the patient should be warned of potential harm to the fetus. Women of childbearing age should be advised to avoid pregnancy while receiving etoposide therapy. It is not known whether etoposide is excreted in human milk; however, because of the potential for HIV transmission and for serious adverse effects to the breast-fed infant if the drug is distributed into milk, women should be instructed not to breast-feed while receiving etoposide therapy.[13]

The metabolic fate of etoposide has not been fully determined. The major urinary metabolite of etoposide is the hydroxy acid 4'-demethylepipodophyllilic acid-9-(4,6-O-(R)-ethylidene-beta-D-glucopyranoside). It is also present in human plasma, presumably as the trans isomer. Glucuronide and sulfate conjugates of etoposide are excreted in human urine and represent 5% to 22% of the dose. O-demethylation of the dimethoxyphenol ring occurs through the CYP3A4 isoenzyme pathway to produce the corresponding catechol.[14]

Metabolism and excretion of etoposide appear to be similar following oral or IV administration. Etoposide and its metabolites are excreted principally in urine; fecal excretion of the drug is variable. Following IV infusion in patients with normal renal and hepatic function, approximately 40% to 60% of a dose is excreted in urine as unchanged drug and metabolites within 48 to 72 hours; less than 2% to 16% is excreted in feces within 24 hours and 30% to 45% within 48 hours. Following oral administration, about 5% to 25% of the dose is excreted in urine within 24 to 48 hours.[15]

Following IV infusion, etoposide disposition has been described as biphasic, although some data indicate triphasic elimination with a prolonged terminal phase. In adults with normal renal and hepatic function, etoposide half-life averages from about 0.6 to 2.0 hours in the initial phase and from 5.3 to 10.8 hours in the terminal phase. In children

with normal renal and hepatic function, etoposide half-life averages from 0.6 to 1.4 hours in the initial phase and from 3 to 5.8 hours in the terminal phase.[16]

Because patients with impaired renal function receiving etoposide have exhibited reduced total body clearance, increased AUC, and lower volume of distribution at steady state, initial dose modification should be considered based on measured creatinine clearance.[17] Reduced plasma clearance and elimination of etoposide has been reported in some patients with impaired hepatic function.[18]

## Adverse Events/Toxicity

---

The most frequent and clinically significant adverse effects of etoposide are hematologic and include anemia, leukopenia, neutropenia, and thrombocytopenia.[19] With leukopenia, the nadir of granulocyte count occurs 7 to 14 days after administration. Recovery is usually complete by the 20th day; cumulative myelosuppression has not been reported.[20]

Other frequently reported but less serious adverse effects include abdominal pain, reversible alopecia, asthenia, anorexia, chills and/or fever, constipation, diarrhea, dizziness, extravasation, malaise, mucositis, nausea and vomiting, phlebitis, pruritus, rash, taste perversion, and urticaria.[21] Localized herpes zoster infections have occurred in a few HIV infected patients being treated with etoposide.[22]

In rare cases, anaphylactic reactions have occurred in patients receiving etoposide. These reactions have been characterized by one or more of the following symptoms: bronchospasm, chills, diaphoresis, dyspnea, fever, pruritus, hypertension or hypotension, loss of consciousness, nausea, rigors, tachycardia, and vomiting. Anaphylactic reactions occurring during initial infusion of etoposide have included back pain, laryngospasm, loss of consciousness, swelling of the face and tongue, and tightness in the throat.[23]

## Drug and Food Interactions

---

High-dose cyclosporine resulting in concentrations above 2000 ng/ml administered with oral etoposide

# Etoposide phosphate

## Drug and Food Interactions (cont.)

has led to an 80% increase in etoposide exposure and a 38% decrease in total body clearance of etoposide compared to etoposide administered alone.[24]

Caution should be used when administering etoposide phosphate with drugs that inhibit phosphatase activities, such as levamisole hydrochloride.[25]

Concurrent use of etoposide with bone marrow depressants or radiation therapy may cause additive bone marrow depression.[26]

Normal immune mechanisms may be suppressed during etoposide therapy, causing a patient's antibody response to a killed virus vaccine to be decreased. In addition, concurrent use of etoposide with a live virus vaccine may enable virus replication, increase adverse effects of the vaccine, or decrease a patient's antibody response to the vaccine. Patients receiving etoposide therapy should therefore avoid any vaccination until etoposide therapy has been discontinued for 3 months to 1 year.[27]

## Contraindications

Etoposide and etoposide phosphate are contraindicated in patients who have demonstrated a previous hypersensitivity to etoposide or any components in the formulations.[28] Risk-benefit of etoposide therapy should be considered with the following medical conditions: bone marrow depression; existing or recent chickenpox; infection; or previous cytotoxic drug therapy.[29]

## Clinical Trials

For information on clinical trials that involve Etoposide phosphate, visit the ClinicalTrials.gov web site at <http://www.clinicaltrials.gov>. In the Search box, enter: Etoposide phosphate AND HIV Infections.

## Dosing Information

Mode of Delivery: Oral; intravenous.[30]

Dosage Form: Etoposide: 50 mg capsules and as multiple-dose vials for injection containing 100 mg/5 ml, 150 mg/7.5 ml, 500 mg/25 ml, or 1 g/50 ml.[31] Etoposide phosphate: 100 mg vials to be reconstituted at concentrations of 10 mg/ml and 20 mg/ml.[32]

Storage: Etoposide capsules must be stored under refrigeration at 2 C to 8 C (36 F to 46 F).[33]

Etoposide phosphate unopened vials should be stored under refrigeration at 2 C to 8 C (36 F to 46 F) and kept in the original package to protect it from light.[34]

## Chemistry

CAS Name: Etoposide:  
4'-Demethylepipodophyllotoxin  
9-[4,6-O-(R)-ethylidene-beta-D-glucopyranoside]  
Etoposide phosphate:  
4'-Demethylepipodophyllotoxin  
9-(4,6-O-(R)-ethylidene-beta-D-glucopyranoside),  
4'-(dihydrogen phosphate) (Etoposide  
phosphate)[35]

CAS Number: Etoposide: 33419-42-0  
Etoposide phosphate: 117091-64-2[36]

Molecular formula: Etoposide: C<sub>29</sub>H<sub>32</sub>O<sub>13</sub> /  
Etoposide phosphate: C<sub>29</sub>H<sub>33</sub>O<sub>16</sub>P[37]

Etoposide: C<sub>59</sub>.18%, H<sub>5</sub>.48%, O<sub>35</sub>.34% /  
Etoposide phosphate: C<sub>52</sub>.10%, H<sub>4</sub>.98%,  
O<sub>38</sub>.29%, P<sub>4</sub>.63% (Calculation)[38]

Molecular weight: Etoposide: 588.56 / Etoposide  
phosphate: 668.54[39]

Melting point: 236-251 C[40]

Stability: Unopened vials of etoposide for injection are stable for 24 months at room temperature (25 C). Vials diluted as recommended to concentrations of 0.2 mg or 0.4 mg/ml are stable for 96 or 24 hours, respectively, at room temperature under normal room fluorescent light in both glass and plastic containers.[41]

Unopened vials of etoposide phosphate for injection are stable until the date indicated on the label if stored under refrigeration at 2 C to 8 C (36

# Etoposide phosphate



## Chemistry (cont.)

---

F to 46 F); at controlled room temperature of 20 C to 25 C (68 F to 77 F) following reconstitution with Sterile Water for Injection, USP, 5% Dextrose Injection, USP, or 0.9% Sodium Chloride Injection, USP; or at controlled room temperature of 20 C to 25 C for 48 hours following reconstitution with Sterile Bacteriostatic Water for Injection with Benzyl Alcohol, USP, or Bacteriostatic Sodium Chloride for Injection with Benzyl Alcohol, USP. Further diluted solutions of etoposide phosphate can be stored under refrigeration at 2 C to 8 C or at controlled room temperature of 20 C to 25 C for 24 hours.[42]

Solubility: Etoposide is very soluble in methanol and in chloroform, slightly soluble in ethanol, and sparingly soluble in water and in ether. It is made more miscible with water by means of organic solvents.[43] Etoposide phosphate is soluble in water and practically insoluble in organic solvents.[44]

## Other Names

---

VP 16213[45]

VP-16[46]

Etopofos (Etoposide phosphosphate)[47]

Lastet[48]

NSC 141540[49]

## Further Reading

---

Fardet L, Blum L, Kerob D, Agbalika F, Galicier L, Dupuy A, Lafaurie M, Meignin V, Morel P, Lebbe C. Human herpesvirus 8-associated hemophagocytic lymphohistiocytosis in human immunodeficiency virus-infected patients. *Clin Infect Dis*. 2003 Jul 15;37(2):285-91. Epub 2003 Jul 01.

Re A, Cattaneo C, Michieli M, Casari S, Spina M, Rupolo M, Allione B, Nosari A, Schiantarelli C, Viganò M, Izzi I, Ferremi P, Lanfranchi A, Mazzuccato M, Carosi G, Tirelli U, Rossi G, Mazzuccato M. High-dose therapy and autologous

peripheral-blood stem-cell transplantation as salvage treatment for HIV-associated lymphoma in patients receiving highly active antiretroviral therapy. *J Clin Oncol*. 2003 Dec 1;21(23):4423-7. Epub 2003 Oct 27. Erratum in: *J Clin Oncol*. 2004 Jan 15;22(2):386. Mazzuccato Maurizio [corrected to Mazzuccato Mauro].

Sparano JA, Lee S, Chen MG, Nazeer T, Einzig A, Ambinder RF, Henry DH, Manalo J, Li T, Von Roenn JH. Phase II trial of infusional cyclophosphamide, doxorubicin, and etoposide in patients with HIV-associated non-Hodgkin's lymphoma: an Eastern Cooperative Oncology Group Trial (E1494). *J Clin Oncol*. 2004 Apr 15;22(8):1491-500.

## Manufacturer Information

---

Etoposide phosphate  
Bristol - Myers Squibb Co  
PO Box 4500  
Princeton, NJ 08543-4500  
(800) 321-1335

VePesid  
Bristol - Myers Squibb Co  
PO Box 4500  
Princeton, NJ 08543-4500  
(800) 321-1335

Toposar  
Pfizer Inc  
235 East 42nd Street  
New York, NY 10017-5755  
(800) 438-1985

Etopophos (phosphate salt)  
Bristol - Myers Squibb Co  
PO Box 4500  
Princeton, NJ 08543-4500  
(800) 321-1335

## For More Information

---

Contact your doctor or an AIDSinfo Health Information Specialist:

- Via Phone: 1-800-448-0440 Monday - Friday,



# Etoposide phosphate



## For More Information (cont.)

---

12:00 p.m. (Noon) - 5:00 p.m. ET

• Via Live Help: [http://aidsinfo.nih.gov/live\\_help](http://aidsinfo.nih.gov/live_help)  
Monday - Friday, 12:00 p.m. (Noon) - 4:00 p.m. ET

## References

---

1. AHFS Drug Information - 2004; p. 985
2. NCT00049439 - Combination chemotherapy in treating patients with AIDS-related non-Hodgkin's lymphoma. National Cancer Institute. Available at: <http://clinicaltrials.gov/ct/show/NCT00049439>. Accessed 7/28/04.
3. NCT00032149 - Combination chemotherapy plus filgrastim in treating patients with HIV-related non-Hodgkin's lymphoma. National Cancer Institute. Available at: <http://clinicaltrials.gov/ct/show/NCT00032149>. Accessed 7/28/04.
4. NCT00049036 - Combination chemotherapy and rituximab in treating patients with HIV-associated non-Hodgkin's lymphoma. National Cancer Institute. Available at: <http://clinicaltrials.gov/ct/show/NCT00049036>. Accessed 7/28/04.
5. NCT00006436 - EPOCH-rituximab to treat non-Hodgkin's lymphoma in patients with HIV infection. National Cancer Institute. Available at: <http://clinicaltrials.gov/ct/show/NCT00006436>. Accessed 7/30/04.
6. USP DI - 2004; p. 1326
7. USP DI - 2004; p. 1326
8. AHFS Drug Information - 2004; p. 990
9. AHFS Drug Information - 2004; p. 990
10. Bristol-Myers Squibb - Etopophos Product Information, p. 1. Available at: [http://www.bms.com/cgi-bin/anybin.pl?sql=select%20PPI%20from%20TB\\_PRODUCT\\_PPI%20where%20PPI\\_SEQ=73&key=PPI](http://www.bms.com/cgi-bin/anybin.pl?sql=select%20PPI%20from%20TB_PRODUCT_PPI%20where%20PPI_SEQ=73&key=PPI). Accessed 7/29/04.
11. AHFS Drug Information - 2004; p. 990
12. AHFS Drug Information - 2004; pp. 990-991
13. Bristol-Myers Squibb - Etopophos Product Information, p. 1. Available at: [http://www.bms.com/cgi-bin/anybin.pl?sql=select%20PPI%20from%20TB\\_PRODUCT\\_PPI%20where%20PPI\\_SEQ=73&key=PPI](http://www.bms.com/cgi-bin/anybin.pl?sql=select%20PPI%20from%20TB_PRODUCT_PPI%20where%20PPI_SEQ=73&key=PPI). Accessed 7/29/04.
14. Bristol-Myers Squibb - Etopophos Product Information, p. 1. Available at: [http://www.bms.com/cgi-bin/anybin.pl?sql=select%20PPI%20from%20TB\\_PRODUCT\\_PPI%20where%20PPI\\_SEQ=73&key=PPI](http://www.bms.com/cgi-bin/anybin.pl?sql=select%20PPI%20from%20TB_PRODUCT_PPI%20where%20PPI_SEQ=73&key=PPI). Accessed 7/29/04.
15. AHFS Drug Information - 2004; p. 991
16. AHFS Drug Information - 2004; p. 991
17. Bristol-Myers Squibb - Etopophos Product Information, p. 1. Available at: [http://www.bms.com/cgi-bin/anybin.pl?sql=select%20PPI%20from%20TB\\_PRODUCT\\_PPI%20where%20PPI\\_SEQ=73&key=PPI](http://www.bms.com/cgi-bin/anybin.pl?sql=select%20PPI%20from%20TB_PRODUCT_PPI%20where%20PPI_SEQ=73&key=PPI). Accessed 7/29/04.
18. AHFS Drug Information - 2004; p. 991
19. Bristol-Myers Squibb - Etopophos Product Information, p. 2. Available at: [http://www.bms.com/cgi-bin/anybin.pl?sql=select%20PPI%20from%20TB\\_PRODUCT\\_PPI%20where%20PPI\\_SEQ=73&key=PPI](http://www.bms.com/cgi-bin/anybin.pl?sql=select%20PPI%20from%20TB_PRODUCT_PPI%20where%20PPI_SEQ=73&key=PPI). Accessed 7/29/04.
20. USP DI - 2004; p. 1328
21. Bristol-Myers Squibb - Etopophos Product Information, p. 2. Available at: [http://www.bms.com/cgi-bin/anybin.pl?sql=select%20PPI%20from%20TB\\_PRODUCT\\_PPI%20where%20PPI\\_SEQ=73&key=PPI](http://www.bms.com/cgi-bin/anybin.pl?sql=select%20PPI%20from%20TB_PRODUCT_PPI%20where%20PPI_SEQ=73&key=PPI). Accessed 7/29/04.
22. AHFS Drug Information - 2004; p. 989
23. Bristol-Myers Squibb - Etopophos Product Information, p. 2. Available at: [http://www.bms.com/cgi-bin/anybin.pl?sql=select%20PPI%20from%20TB\\_PRODUCT\\_PPI%20where%20PPI\\_SEQ=73&key=PPI](http://www.bms.com/cgi-bin/anybin.pl?sql=select%20PPI%20from%20TB_PRODUCT_PPI%20where%20PPI_SEQ=73&key=PPI). Accessed 7/29/04.

# Etoposide phosphate



24. Bristol-Myers Squibb - Etopophos Product Information, p. 1. Available at:  
[http://www.bms.com/cgi-bin/anybin.pl?sql=select%20PPI%20from%20TB\\_PRODUCT\\_PPI%20where%20PPI\\_SEQ=73&key=PPI](http://www.bms.com/cgi-bin/anybin.pl?sql=select%20PPI%20from%20TB_PRODUCT_PPI%20where%20PPI_SEQ=73&key=PPI). Accessed 7/29/04.
25. Bristol-Myers Squibb - Etopophos Product Information, p. 1. Available at:  
[http://www.bms.com/cgi-bin/anybin.pl?sql=select%20PPI%20from%20TB\\_PRODUCT\\_PPI%20where%20PPI\\_SEQ=73&key=PPI](http://www.bms.com/cgi-bin/anybin.pl?sql=select%20PPI%20from%20TB_PRODUCT_PPI%20where%20PPI_SEQ=73&key=PPI). Accessed 7/29/04.
26. USP DI - 2004; p. 1327
27. USP DI - 2004; p. 1327
28. Bristol-Myers Squibb - Etopophos Product Information, p. 1. Available at:  
[http://www.bms.com/cgi-bin/anybin.pl?sql=select%20PPI%20from%20TB\\_PRODUCT\\_PPI%20where%20PPI\\_SEQ=73&key=PPI](http://www.bms.com/cgi-bin/anybin.pl?sql=select%20PPI%20from%20TB_PRODUCT_PPI%20where%20PPI_SEQ=73&key=PPI). Accessed 7/29/04.
29. USP DI - 2004; pp. 1327-1328
30. USP DI - 2004; pp. 1329-1330
31. Bristol-Myers Squibb - VePesid Product Information, p. 2. Available at:  
[http://www.bms.com/cgi-bin/anybin.pl?sql=select%20PPI%20from%20TB\\_PRODUCT\\_PPI%20where%20PPI\\_SEQ=20&key=PPI](http://www.bms.com/cgi-bin/anybin.pl?sql=select%20PPI%20from%20TB_PRODUCT_PPI%20where%20PPI_SEQ=20&key=PPI). Accessed 7/29/04.
32. Bristol-Myers Squibb - Etopophos Product Information, p. 2. Available at:  
[http://www.bms.com/cgi-bin/anybin.pl?sql=select%20PPI%20from%20TB\\_PRODUCT\\_PPI%20where%20PPI\\_SEQ=73&key=PPI](http://www.bms.com/cgi-bin/anybin.pl?sql=select%20PPI%20from%20TB_PRODUCT_PPI%20where%20PPI_SEQ=73&key=PPI). Accessed 7/29/04.
33. Bristol-Myers Squibb - VePesid Product Information, p. 2. Available at:  
[http://www.bms.com/cgi-bin/anybin.pl?sql=select%20PPI%20from%20TB\\_PRODUCT\\_PPI%20where%20PPI\\_SEQ=20&key=PPI](http://www.bms.com/cgi-bin/anybin.pl?sql=select%20PPI%20from%20TB_PRODUCT_PPI%20where%20PPI_SEQ=20&key=PPI). Accessed 7/29/04.
34. Bristol-Myers Squibb - Etopophos Product Information, p. 2. Available at:  
[http://www.bms.com/cgi-bin/anybin.pl?sql=select%20PPI%20from%20TB\\_PRODUCT\\_PPI%20where%20PPI\\_SEQ=73&key=PPI](http://www.bms.com/cgi-bin/anybin.pl?sql=select%20PPI%20from%20TB_PRODUCT_PPI%20where%20PPI_SEQ=73&key=PPI). Accessed 8/5/04.
35. ChemIDplus - Available at: <http://chem.sis.nlm.nih.gov/chemidplus/>. Accessed 7/29/04.
36. ChemIDplus - Available at: <http://chem.sis.nlm.nih.gov/chemidplus/>. Accessed 7/29/04.
37. ChemIDplus - Available at: <http://chem.sis.nlm.nih.gov/chemidplus/>. Accessed 7/29/04.
38. Merck Index - 2001; p. 687
39. Merck Index - 2001; p. 351
40. Merck Index - 2001; p. 688
41. Bristol-Myers Squibb - VePesid Product Information, p. 2. Available at:  
[http://www.bms.com/cgi-bin/anybin.pl?sql=select%20PPI%20from%20TB\\_PRODUCT\\_PPI%20where%20PPI\\_SEQ=20&key=PPI](http://www.bms.com/cgi-bin/anybin.pl?sql=select%20PPI%20from%20TB_PRODUCT_PPI%20where%20PPI_SEQ=20&key=PPI). Accessed 7/29/04.
42. Bristol-Myers Squibb - Etopophos Product Information, p. 2. Available at:  
[http://www.bms.com/cgi-bin/anybin.pl?sql=select%20PPI%20from%20TB\\_PRODUCT\\_PPI%20where%20PPI\\_SEQ=73&key=PPI](http://www.bms.com/cgi-bin/anybin.pl?sql=select%20PPI%20from%20TB_PRODUCT_PPI%20where%20PPI_SEQ=73&key=PPI). Accessed 7/29/04.
43. Bristol-Myers Squibb - VePesid Product Information, p. 1. Available at:  
[http://www.bms.com/cgi-bin/anybin.pl?sql=select%20PPI%20from%20TB\\_PRODUCT\\_PPI%20where%20PPI\\_SEQ=20&key=PPI](http://www.bms.com/cgi-bin/anybin.pl?sql=select%20PPI%20from%20TB_PRODUCT_PPI%20where%20PPI_SEQ=20&key=PPI). Accessed 8/2/04.
44. Merck Index - 2001; p. 688
45. ChemIDplus - Available at: <http://chem.sis.nlm.nih.gov/chemidplus/>. Accessed 8/2/04.
46. ChemIDplus - Available at: <http://chem.sis.nlm.nih.gov/chemidplus/>. Accessed 8/2/04.
47. ChemIDplus - Available at: <http://chem.sis.nlm.nih.gov/chemidplus/>. Accessed 8/2/04.
48. ChemIDplus - Available at: <http://chem.sis.nlm.nih.gov/chemidplus/>. Accessed 8/2/04.
49. ChemIDplus - Available at: <http://chem.sis.nlm.nih.gov/chemidplus/>. Accessed 8/2/04.